Remarks:

Claims 1-7 are pending in the present application, and claims 11-14 have been withdrawn from consideration. By this Amendment, claims 11-14 are canceled. Claim 1 is amended. Support for the amendments to the claims are found in the specification as originally filed, as the amendment to claim 1 clarifies that the time period referred to in step a) is between 1.5 and 3.5 hours, inclusive . No new matter is added to the claims by these amendments. Accordingly, entry of the amendments to the claims is respectfully requested.

Claim objections:

Claims 1-7 were objected for lacking an appropriate opening phrase for the listing of claims. The specification has been amended to incorporate the appropriate language. No new matter is added by this amendment. Therefore, withdrawal of the objection to claims 1-7 is respectfully requested.

Claim Rejections under 35 U.S.C. 102:

Claims 1-3, 5, and 6 were rejected under 35 U.S.C. 102(b) as anticipated by Grunau et al. (Nucleic Acids Res. (2001) 29:e65, 1-7). The Office Action states that Grunau et al. teaches a method for the conversion of a cytosine base in an oligonucleotide solution to a uracil base, comprising incubating the solution between 70 and 90 °C. The Office Action argues that by teaching incubation of the solution for a period of four hours, the claim limitation of "incubating a solution comprising the nucleic acid for a time period of 1.5 to 3.5 hours" is met, as incubating solution for four hours necessarily involves incubating the solution for between 1.5 and 3.5 hours.

Applicants have amended claim 1 to recite "incubating a solution comprising the nucleic acid for a time period that is not less than 1.5 hours and further is not more than 3.5 hours". Incubation of a solution for periods of one hour or of four hours, as taught by Grunau et al., does not anticipate the claimed limitation, because incubation for one hour is less than 1.5 hours and incubation for four hours is more than 3.5 hours. This element is neither taught nor suggested by Grunau et al. Accordingly, reconsideration and withdrawal of the rejection of claims 1-3, 5, and 6 under 35 U.S.C. 102(b) is respectfully requested.

Claim Rejections under 35 U.S.C. 103(a):

Claim 4 was rejected under under 35 U.S.C. 103(a) as obvious over Grunau et al. in view of Hayatsu et al. (Biochemistry (1970) 9:2858-2865). Claim 7 was rejected as obvious over Grunau et al. in view of Hayatsu et al. and further in view of Olek et al. (Nucleic Acids Res. (1996) 24:5064-5066).

Claims 4 and 7 depend from claim 1, and therefore incorporate all the limitations present in those claims. As noted above, Grunau et al. neither teaches nor suggests an element of the claims as amended. Furthermore, none of the other references cited in the Action teach or suggest the limitation "incubating a solution comprising the nucleic acid for a time period that is not less than 1.5 hours and further is not more than 3.5 hours". The Office Action relies on the secondary references to support an argument relating not to the length of the incubation, but to the pH range in which the incubations were performed. Accordingly, Applicants respectfully submit that the cited combination of references does not support a *prima facie* case of obviousness of claims 4 and 7.

Applicants further submit that the claimed range for length of incubation is not mere optimization of a previously known range, because in this instance there is no motivation to optimize the range. Grunau et al. explicitly teaches states that they optimized the conditions for selective deamination of cytosine to uracil (Abstract; page 1/7, col. 2 – "Over the last few years, several groups have studied the original reaction conditions and suggested technical improvements (references). However, some of these observations are controversial and no comprehensive investigation of all the parameters has been accomplished so far. Since the method is based on the complete conversion of cytosine and the complete non-conversion of 5mC, we decided to quantify and to compare the sensitivity and specificity at different time/temperature combinations for the incubation with bisulfite."...We present in this work for the first time a comprehensive investigation of the influence of time and temperature of the bisulfite reaction on the sensititivity and specificity of the bisulfite sequencing method and deliver an estimation of the degree of DNA degradation during the treatment."; page 3/7, col. 2 – "The optimal bisulfite genomic sequencing method must deliver complete conversion of cytosine residues to uracil while the minor base 5mC should remain intact. In addition, the loss of DNA during the modification reaction due to non-specific degradation should be kept as small as possible."; page 6/7, col. 2 – "Our work delivers for the first time a comprehensive description of the influence of the most critical reaction parameters. This improves the scientific basis of this technique and will help avoid potential error sources in the experimental setup." In view of the fact that the cited reference teaches optimization of the conditions for selective deamination of cytosine to uracil were achieved, what would be

the motivation for further investigating the very same conditions investigated by the authors of the reference? Accordingly, reconsideration and withdrawal of the rejections of claims 4, 6-9, 14 and 15 under 35 U.S.C. 103(a) are respectfully requested.

Conclusion:

In view of the above, Applicants believe all claims now pending in this Application are in condition for allowance. Applicants hereby request a three-month extension of time for responding to the Office Action. The Commissioner is hereby authorized to charge the extension of time fee (large entity) under 37 CFR 1.17 to Account No. 50-0812. The Commissioner is further authorized to charge any fee deficiency, or credit any overpayment, to Deposit Account No. 50-0812.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned directly at 510-814-2891.

Respectfully submitted,

Date: March 16, 2007

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